Multiscale computational models for optogenetic control of cardiac function.

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Public Summary:
The ability to stimulate mammalian cells with light has significantly changed our understanding of electrically excitable tissues in health and disease, paving the way toward various novel therapeutic applications. Here, we demonstrate the potential of optogenetic control in cardiac cells using a hybrid experimental/computational technique. Experimentally, we introduced channelrhodopsin-2 into undifferentiated human embryonic stem cells via a lentiviral vector, and sorted and expanded the genetically engineered cells. Via directed differentiation, we created channelrhodopsin-expressing cardiomyocytes, which we subjected to optical stimulation. To quantify the impact of photostimulation, we assessed electrical, biochemical, and mechanical signals using patch-clamping, multielectrode array recordings, and video microscopy. Computationally, we introduced channelrhodopsin-2 into a classic autorhythmic cardiac cell model via an additional photocurrent governed by a light-sensitive gating variable. Upon optical stimulation, the channel opens and allows sodium ions to enter the cell, inducing a fast upstroke of the transmembrane potential. We calibrated the channelrhodopsin-expressing cell model using single action potential readings for different photostimulation amplitudes, pulse widths, and frequencies. To illustrate the potential of the proposed approach, we virtually injected channelrhodopsin-expressing cells into different locations of a human heart, and explored its activation sequences upon optical stimulation. Our experimentally calibrated computational toolbox allows us to virtually probe landscapes of process parameters, and identify optimal photostimulation sequences toward pacing hearts with light.

Scientific Abstract:
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